

Claims

1. A method of detecting an HPV-induced invasive cancer or precursor lesion thereof associated with tumor suppressor lung cancer 1 (TSLC1) in a subject in need thereof, said method comprising contacting a cell component of a test cell of the subject with a reagent that detects the level of the cell component in the test cell and determining a modification in the level of the cell component in the test cell as compared with a comparable healthy cell, wherein the cell component indicates the level of TSLC1 in the cell and wherein a decrease in the level of TSLC1 indicates the presence of an HPV-induced invasive cancer or precursor lesion thereof.
2. Method according to claim 1, wherein said HPV-induced invasive cancer or precursor lesion thereof is invasive cervical cancer or a premalignant cervical lesion with invasive potential.
3. Method according to claim 1 or 2, wherein said HPV-induced invasive cancer is a high-risk HPV-induced invasive cancer.
4. Method according to any one of the preceding claims, wherein the cell component is a nucleic acid associated with production of TSLC1 polypeptide and the reagent targets the nucleic acid in the test cell, said nucleic acid preferably encoding the TSLC1 and regulatory regions.
5. Method according to claims 4, wherein the nucleic acid is RNA, preferably mRNA.
6. Method according to any one of the preceding claims, wherein the reagent is a restriction endonuclease, preferably a methylation sensitive restriction endonuclease.
7. Method according to claim 5, wherein the reagent is a nucleic acid probe or primer that binds to the nucleic acid, said nucleic acid probe or primer preferably having a detectable label.
8. Method according to claim 7, wherein the nucleic acid probe has a nucleotide sequence selected from the group consisting of:

a) a polynucleotide sequence capable of hybridizing under stringent conditions to the 5' regulatory region or the coding region of the *TSLC1* sequence as set forth in Figure 1;

5 b) a polynucleotide having at least 70% identity to the polynucleotide of a);

c) a polynucleotide complementary to the polynucleotide of a); and

d) a polynucleotide comprising at least 15 bases of a nucleotide of a) or b).

9. Method according to any one of the claims 1-4, wherein the cell
10 component is a polypeptide and the reagent targets the polypeptide in the test cell, said polypeptide preferably being *TSLC1* and said reagent preferably being an anti-*TSLC1* antibody.

10. Method according to any one of the claims 1-5, wherein said method of detecting evaluates the methylation status of the *TSLC1* promoter.

15 11. A method of detecting HPV-induced invasive cancer or precursor lesion thereof associated with tumor suppressor lung cancer 1 (*TSLC1*) in a subject in need thereof, said method comprising contacting a target cellular component of a test cell with a reagent that detects *TSLC1* and detecting a reduction in the *TSLC1* as compared to that of a comparable normal cell,
20 preferably in said detection an increased methylation of the *TSLC1* promoter in the test cell and/or a reduced production of *TSLC1* in the test cell as compared to the comparable normal cell is determined.

12. Method according to claim 11, wherein the target cellular component is nucleic acid.

25 13. Method according to claim 12, wherein the nucleic acid is RNA, preferably mRNA.

14. Method according to claim 11, wherein the target cellular component is a protein.

15. Method according to claim 12 or 13, wherein the reagent is a nucleic acid probe or primer that binds to *TSLC1*.
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16. Method according to claim 14, wherein the reagent is an anti-TSLC1 antibody.
17. Method according to any one of the claims 11-16, wherein subject has loss of heterozygosity at chromosome 11q23.
- 5 18. A method of treating HPV-induced invasive cancers and their precursor lesions associated with modification of TSLC1 production in cells in a subject in need thereof, said method comprising contacting said cells of a patient suffering from said cancer with a therapeutically effective amount of a reagent that increases TSLC1 level in said cells.
- 10 19. Method according to claim 18, wherein the reagent is a polynucleotide sequence comprising a TSLC1 sense polynucleotide sequence, preferably said polynucleotide is the native, unmethylated TSLC1 sense sequence.
- 15 20. Method according to claim 19, wherein a nonmethylatable analog is substituted for cytidine within the TSLC1 sense sequence, said nonmethylatable analog preferably being is 5-azacytadine.
21. Method according to claim 19 or 20, wherein said polynucleotide sequence is contained in an expression vector, said expression vector preferably being a plasmid, a viral particle or a phage.
- 20 22. Use of a molecular diagnostic marker for detection of progression to invasiveness of HPV-induced premalignant lesions associated with tumor suppressor lung cancer 1 (TSLC1) and for detection of future metastatic potential of HPV-induced premalignant lesions and carcinomas associated with tumor suppressor lung cancer 1 (TSLC1), wherein said marker indicates
- 25 *TSLC1* promoter methylation and/or expression of mRNA associated with production of TSLC1 polypeptide.
23. Kit of parts for use in a method of detecting HPV-induced invasive cancers and their precursor associated with tumor suppressor lung cancer 1 (TSLC1) in test cells of a subject, said kit comprising means to collect test cells

and means for the detection of *TSLC1* promoter methylation or *TSLC1* expression.

24. Kit of parts for use in a method of detecting HPV-induced invasive cancers and their precursor lesions associated with tumor suppressor lung cancer 1 (*TSLC1*) in test cells of a subject, said kit comprising primers and probes capable of hybridising to *TSLC1* nucleotide sequence of Figure 1, *TSLC1* antibodies, or methylation sensitive restriction enzymes recognizing the sequence as described in Figure 1.

25. Kit of parts according to claim 23 or 24, wherein the test cells are cervical cells.